The Sapphire Group™

30 April 2007

VIA EMAIL: shane@niehs.nih.gov
Dr. Barbara Shane
Executive Secretary for the NTP Board
NTP Liaison and Scientific Review Office
NIEHS
P.O. Box 12233
MD A3-01
Research Triangle Park, NC 27709

Re: Public Comment to NTP Draft Technical Report (NTP TR 546: Sodium Dichromate Dihydrate)

Dear Dr. Shane:

At the request of PPG Industries, *The Sapphire Group, Inc.* has reviewed the document entitled, "*NTP Technical Report on the Toxicology and Carcinogenesis of Sodium Dichromate Dihydrate (CAS No. 7789-12-0) in F344N Rats and B6C3F1 Mice (Drinking Water Studies)*", designated NTP TR 546, NIH Publication No. 07-5887. The comments presented below are in response to the invitation for public comment listed in the Federal Register Notice of 2 March 2007 (pages 9546-9547).

Comment 1:
The draft report indicates that histiocytic infiltration was consistently observed in several tissues in rats and mice exposed for 2 years and that the significance of these lesions is not known. We ask that the review panel discuss this finding in more depth and offer some indication of what this finding might mean regarding the tumors observed in this study.

Comment 2:
The tumors found in the oral cavities of rats indicate to us that the capacity of rat saliva to reduce hexavalent chromium to trivalent chromium was likely surpassed. The observation that there were no tumors seen in the rat stomach or small intestines indicates that the reducing capacities of these organs were sufficient to reduce any hexavalent chromium that escaped

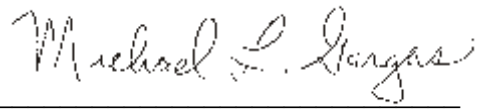
reduction while in the oral cavity. What is perplexing is the observation of tumors in the small intestines of mice, with no tumors observed in the stomach or oral cavities. It seems odd that hexavalent chromium would be present (unreduced) in the small intestines of these mice and be available to exert a tumor response, while producing no such response in the stomach and oral cavity, where presumably, chromium in the hexavalent state should also have been present. We would be interested in discussions by the review panel on this curious finding.

Comment 3:

The interpretation offered in the draft report regarding the comparison of tissue distribution of chromium in this present study and the study involving chromium picolinate needs to be clarified. According to the legend of Figure 7 (page 88), a comparison is made between the chromium administered during weeks 1-25 at the 2000 ppm level in the chromium picolinate study (8.95 mg Cr/kg body weight), and that administered during weeks 1-25 of the sodium dichromate dihydrate study at the 516 mg/L dosing level (152 mg Cr/kg body weight). This calculates as about a 17 fold difference in chromium dose, with hexavalent chromium being higher than trivalent chromium. The text on page 87 indicates that according to Figure 7, more chromium is taken up into each tissue when hexavalent chromium is administered compared to trivalent chromium (e.g. chromium picolinate), ranging from 5 to 16 fold higher. It seems to us that the difference in total administered dose between the trivalent chromium and the hexavalent chromium (17 fold) is reflected in the differences in tissue concentrations (5-16 fold), and may not be reflective of an increased absorption of the hexavalent chromium as is suggested in the text. It is difficult for us to investigate this further until the corresponding tables from the chromium picolinate study become available, but it would be helpful if the review panel were able to clarify this result and conclusion during their discussions at the upcoming review meeting.

Thank you for the opportunity to provide these comments.

Sincerely,



Michael L. Gargas, Ph.D.
Managing Principal